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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/973,303	11/28/1997	PETER DORMER	3428-005	6732
21967	7590	01/14/2004	EXAMINER	
HUNTON & WILLIAMS LLP INTELLECTUAL PROPERTY DEPARTMENT 1900 K STREET, N.W. SUITE 1200 WASHINGTON, DC 20006-1109			CANELLA, KAREN A	
			ART UNIT	PAPER NUMBER
			1642	
DATE MAILED: 01/14/2004				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/973,303	DORMER, PETER	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 36, 42, 48-65, 73 and 74 is/are pending in the application.
 4a) Of the above claim(s) 48-61 and 63-65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) 36, 42, 62, 73, 74 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____. |

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DETAILED ACTION

1. Claims 1-35, 37-41, 43-47 and 66-72 are canceled. Claims 36, 42 and 62 have been amended. Claims 73 and 74 are added. Claims 48-61, 63-65, drawn to non-elected inventions, remain withdrawn from consideration. Claims 36, 42, 48-65, 73 and 74 are pending. Claims 36, 42, 62, 73 and 74 are under consideration.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. Claims 36, 42, 62, 73 and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 73 recite "amino acid sequence corresponding to SEQ ID NO:5". It is unclear how an amino acid sequence corresponding to SEQ ID NO:5 differs from the amino acid sequence of SEQ ID NO:5. Applicant is advised to state amino acid sequence consisting of, or comprising SEQ ID NO:5.

Claims 36 and 73 state cDNA comprising SEQ ID NO:6 or 7, or a combination thereof. The metes and bounds of combination thereof cannot be determined because it is unclear if the combination reference to a combination of individual nucleic acid base, or a combination of partial sequences of SEQ ID NO:6 and 7, or a combination of the complete sequence of SEQ ID NO:6 and 7.

Claim 36 recites "stringent hybridization conditions" without reciting the physical and chemical parameters of said conditions.

4. Claims 36, 42, 62, 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 36 has been amended to recite "encoded by a cDNA Sequence

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comprising SEQ ID NO:6 or 7 or a combination thereof. New claim 73 incorporates the same limitation. When given the broadest reasonable interpretation, the combination thereof reads on a combination of individual nucleic acid base, or a combination of partial sequences of SEQ ID NO:6 and 7, or a combination of the complete sequence of SEQ ID NO:6 and 7. The specification as filed does not provide support for said DNA species. One of skill in the art would reasonably conclude that applicant was not in possession of the claimed invention.

Claim 73 is drawn to an isolated protein comprising all of the following properties of a through c. Part c (i) comprises the specific limitation of an amino acid sequence encoded by SEQ ID NO:4; part (ii) comprises the specific limitation of an amino acid sequence which is encoded by cDNA hybridizing to the cDNA of SEQ ID NO:4; part (iii) comprises the specific limitation of an amino acid sequence corresponding to SEQ ID NO:5, and part (iv) comprises the specific limitation of variants of the amino acid sequence corresponding to SEQ ID NO:5. The specification does not provide support for a chimeric molecule comprising all of the limitations of sections (i) through (iv). applicant is advised to modify part c to state "an amino acid sequence selected from the group consisting of" in order to overcome this rejection.

5. Claims 36, 42, 62, 73 and 74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an amino acid sequence which is encoded by a cDNA hybridizing to the complete complement of SEQ ID NO:4 under stringent hybridization conditions, does not reasonably provide enablement for an amino acid sequence which is encoded by a cDNA hybridizing to SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Section c(ii) of claims 36 and 73 are drawn to an amino acid sequence which is encoded by a cDNA which hybridizes to the cDNA of SEQ ID NO:4. The claimed amino acid sequence would not have any similarity to the protein encoded by SEQ ID NO:4 because it would be the complementary sequence and thus translation would begin from the opposite end of said sequence. The specification has not taught how to use said amino acid sequence as it would not be expected that said amino acid would cause the differentiation of Friend Leukemia Cell Lines.

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6. The rejection of claims 36, 42 and 62 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for proteins and fusion proteins comprising SEQ ID NO:2 or SEQ ID NO:4, does not reasonably provide enablement for other proteins which can be cloned from the eda activity characterized in that the differentiation inducing activity is dependent on a serum factor in fetal calf serum and characterized by an increase in mRNA species having variable 5' regions and 3' regions corresponding to the coding regions of SEQ ID NO:2 or therapeutic compositions comprising SEQ ID NO:2, or 4, or variants or fragments of SEQ ID NO:2, or 4 is maintained for the following reasons of record. New claims 73 and 74 are also rejected for the same reasons of record.

There is no objective evidence in the specification that the peptides encoded by SEQ ID NO:6 and 7, which are fragments of SEQ ID NO:2 and 4, can function as a differentiation-inducing activity independently of the complete amino acid sequence of SEQ ID NO:2 and 4, or that other proteins which comprise polynucleotides containing SEQ ID NO:6 and 7 would also have differentiation inducing activity. The specification does not provide any evidence that the peptides encoded by nucleotides 467 to 509 and 523 to 577 of SEQ ID NO:2 would retain the differentiation inducing activity on Friend Leukemia cells, alone, or in the context of a heterologous amino acid sequence. It is well known in the art that proteins are folded 3 dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165 171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3 dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). The specific conformation of a protein results from non covalent interactions between amino acids, beyond what is dictated by the primary amino acid sequence. A different amino acid sequence surrounding the fragments encoded by SEQ ID NO:6 and 7 can potentially radically alter the three dimensional structural environment in which the given fragment is located (Matthews, B. Genetic and Structural Analysis of the Protein Stability Problem, In: Perspectives in Biochemistry, Hans Neurath, Ed., 1989, Vol. 1, pp. 6-9) thus, the consequences of the altered sequence environment cannot be predicted. Additionally, the proteins encoded by SEQ ID NO:2 and 4 are secreted into the cell culture medium, but the instant claims are not limited to secreted proteins. It is recognized in the art that protein function is context dependent, and cellular aspects, such as membrane anchorage, protein activation and sub cellular location must be considered with respect to protein function in addition to molecular aspects (Bork, Genome research, 2000, Vol. 10, pp. 398-400, especially page. 398, under the heading "Limitations in the Total Knowledge Base of Protein Function"). Thus, it is reasonable to conclude that possession of SEQ ID NO:6 and 7, or the other claimed fragments of SEQ ID NO:8-10, would not guarantee that a membrane bound protein would exert that same differentiation inducing activity as the proteins encoded by SEQ ID NO:2 and 4.

Applicant argues that due to the size limitation of the encoded amino acid sequence (section b), it is not possible that SEQ ID NO:6 or 7 alone could fulfill the specific limitation of the claims. This has been considered but not found persuasive. The section of the claims drawn to variants minimally comprise SEQ ID NO:6 or 7. The specification has not taught how to preserve the differentiation inducing ability with hemoglobin formation on Friend Leukemia cells using proteins variants of SEQ ID NO:5 which minimally comprise SEQ ID NO:6 or SEQ ID NO:7. The scope of enablement must be commensurate with the scope of the claims. It is noted that there is no limitation to the number of amino acid substitutions, deletions or additions

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that can be tolerated in a variant of SEQ ID NO:5 that is encoded by a polynucleotide sequence which minimally comprises SEQ ID NO:6 or 7.


7. All other rejections and objections as stated in the previous Office Action are withdrawn.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308.8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308 3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308 0196.


Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

01/12/04